

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

Amendments to the Claims:

Please cancel claims 105-115 and 138-147. This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1.-115. (Cancelled)

116. (Currently amended) A method for producing a human monoclonal antibody that competes for binding to CTLA-4 with an antibody comprising the heavy chain CDR amino acid sequences in SEQ ID NO: 1 and the light chain CDR amino acid sequences in SEQ ID NO: 14 wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and B7-2, said method comprising the steps of:

(a) expressing said competing human monoclonal antibody in a mammalian host cell comprising polynucleotides encoding the heavy and light chains of said competing antibody; and

(b) recovering said competing antibody ~~from said cell~~.

117. (Previously Presented) The method according to claim 116, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with and IC_{50} of 100 nM or less.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

118. (Previously Presented) The method according to claim 116, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 with an IC_{50} of 5 nM or less.

119. (Previously Presented) The method according to claim 116, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 with an IC_{50} of 2 nM or less.

120. (Previously Presented) The method according to claim 116, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-2 with an IC_{50} of 5 nM or less.

121. (Previously Presented) The method according to claim 116, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-2 with an IC_{50} of 2 nM or less.

122. (Previously Presented) The method according to claim 116, wherein a glutamine synthetase expression system is employed in said step of expressing said competing antibody.

123. (Previously Presented) The method according to claim 116, wherein said mammalian cell is a CHO cell.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

124. (Currently amended) The method according to claim 116, wherein said mammalian cell is an NS0Q cell.

125. (Previously Presented) The method according to claim 116, wherein said light chain of said competing antibody utilizes a human A27 V κ gene.

126. (Previously Presented) The method according to claim 116, wherein said polynucleotides encode the heavy and light chain CDRs of a competing antibody that was generated in a mouse whose genome comprises human immunoglobulin genes.

127. (Currently amended) A method for producing a human monoclonal antibody that competes for binding to CTLA-4 with an antibody comprising the heavy chain variable region amino acid sequence in SEQ ID NO: 1, ~~without the signal sequence,~~ and the light chain variable region amino acid sequence in SEQ ID NO: 14, ~~without the signal sequence,~~ wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and B7-2, said method comprising the steps of:

(a) expressing said competing human monoclonal antibody in a mammalian host cell comprising polynucleotides encoding the heavy and light chains of said competing antibody; and

(b) recovering said competing antibody.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

128. (Currently amended) The method according to claim 127, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with an IC₅₀ of 100 nM or less.

129. (Previously presented) The method according to claim 127, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 with an IC₅₀ of 5 nM or less.

130. (Previously presented) The method according to claim 127, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 with an IC₅₀ of 2 nM or less.

131. (Previously presented) The method according to claim 127, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-2 with an IC₅₀ of 5 nM or less.

132. (Previously presented) The method according to claim 127, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-2 with an IC₅₀ of 2 nM or less.

133. (Previously presented) The method according to claim 127, wherein a glutamine synthetase expression system is employed in said step of expressing said competing antibody.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

134. (Previously presented) The method according to claim 127, wherein said mammalian cell is a CHO cell.

135. (Currently amended) The method according to claim 127, wherein said mammalian cell is an NSO cell.

136. (Previously presented) The method according to claim 127, wherein said light chain of said competing antibody utilizes a human A27 V κ gene.

137. (Previously presented) The method according to claim 127, wherein said polynucleotides encode the heavy and light chain CDRs of a competing antibody that was generated in a mouse whose genome comprises human immunoglobulin genes

138.-147. (Cancelled)

148. (Previously presented) A method for producing a human monoclonal antibody that specifically binds to CTLA-4, wherein said antibody comprises a light chain that utilizes a human A27 V κ gene and inhibits binding of human CTLA-4 to human B7-1 and B7-2, said method comprising the steps of:

- (a) expressing said antibody in a mammalian host cell comprising polynucleotides encoding the heavy and light chains of said antibody,
- (b) recovering said antibody.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

149. (Currently amended) The method according to claim 148, wherein said antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with an IC_{50} of 100 nM or less.

150. (Previously presented) The method according to claim 148, wherein said antibody inhibits binding of human CTLA-4 to human B7-1 with an IC_{50} of 5 nM or less.

151. (Previously presented) The method according to claim 148, wherein said antibody inhibits binding of human CTLA-4 to human B7-1 with an IC_{50} of 2 nM or less.

152. (Previously presented) The method according to claim 148, wherein said antibody inhibits binding of human CTLA-4 to human B7-2 with an IC_{50} of 5 nM or less.

153. (Previously presented) The method according to claim 148, wherein said antibody inhibits binding of human CTLA-4 to human B7-2 with an IC_{50} of 2 nM or less.

154. (Previously presented) The method according to claim 148, wherein a glutamine synthetase expression system is employed in said step of expressing said antibody.

155. (Previously presented) The method according to claim 148, wherein said mammalian cell is a CHO cell.

156. (Currently amended) The method according to claim 148, wherein said mammalian cell is an NS0Q cell.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

157. (Previously presented) A method for producing a human monoclonal antibody that specifically binds to CTLA-4, wherein said antibody comprises a light chain that utilizes a human A27 V κ gene and inhibits binding of human CTLA-4 to human B7-1 and B7-2, said method comprising the steps of:

- (a) culturing a host cell comprising polynucleotides encoding the heavy and light chains of said antibody; and
- (b) recovering said antibody.

158. (Currently amended) The method according to claim 157, wherein said antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with an IC_{50} of 100 nM or less.

159. (Previously presented) The method according to claim 157, wherein said antibody inhibits binding of human CTLA-4 to human B7-1 with an IC_{50} of 5 nM or less.

160. (Previously presented) The method according to claim 157, wherein said antibody inhibits binding of human CTLA-4 to human B7-1 with an IC_{50} of 2 nM or less.

161. (Previously presented) The method according to claim 157, wherein said antibody inhibits binding of human CTLA-4 to human B7-2 with an IC_{50} of 5 nM or less.

162. (Previously presented) The method according to claim 157, wherein said antibody inhibits binding of human CTLA-4 to human B7-2 with an IC_{50} of 2 nM or less.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

163. (Previously presented) The method according to claim 157, wherein a glutamine synthetase expression system is employed in said step of expressing said antibody.

164. (Currently amended) A method for producing a human monoclonal antibody that competes for binding to CTLA-4 with an antibody comprising the heavy chain variable region amino acid sequence in SEQ ID NO: 1, ~~without the signal sequence~~, and the light chain variable region amino acid sequence in SEQ ID NO: 14, ~~without the signal sequence~~, wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and B7-2, said method comprising the steps of:

- (a) expressing said competing antibody in a host cell comprising polynucleotides encoding the heavy and light chains of said competing antibody,
- (b) recovering said competing antibody.

165. (Currently amended) The method according to claim 164, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with an IC50 of 100 nM or less.

166. (Previously presented) The method according to claim 164, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 with an IC50 of 5 nM or less.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

167. (Previously presented) The method according to claim 164, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 with an IC₅₀ of 2 nM or less.

168. (Previously presented) The method according to claim 164, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-2 with an IC₅₀ of 5 nM or less.

169. (Previously presented) The method according to claim 164, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-2 with an IC₅₀ of 2 nM or less.

170. (Previously presented) The method according to claim 164, wherein said light chain of said competing antibody utilizes a human A27 V_K gene.

171. (Previously presented) The method according to claim 164, wherein a glutamine synthetase expression system is employed in said step of expressing said antibody.

172. (Previously presented) A method for producing a human monoclonal antibody that specifically binds to CTLA-4, wherein said antibody possesses a selectivity for CTLA-4 over CD28, B7-2, CD44, and hIgG1 of greater than 100:1 and inhibits binding between CTLA-4 and B7-2 with an IC₅₀ of lower than 5 nM; said method comprising the steps of:

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

- (a) expressing said antibody in a mammalian host cell comprising polynucleotides encoding the heavy and light chains of said antibody,
- (b) recovering said antibody.

173. (Previously presented) The method according to claim 172, wherein said antibody inhibits binding of human CTLA-4 to human B7-2 with an IC_{50} of 2 nM or less.

174. (Previously presented) The method according to claim 172, wherein said light chain of said antibody utilizes a human A27 V κ gene.

175. (Previously presented) The method according to claim 172, wherein said polynucleotides encode the heavy and light chain CDRs of an antibody that was generated in a mouse whose genome comprises human immunoglobulin genes.

176. (Previously presented) The method according to claim 172, wherein a glutamine synthetase expression system is employed in said step of expressing said antibody.

177. (New) The method according to claim 176, wherein said mammalian cell is a CHO cell.

178. (New) The method according to claim 176, wherein said mammalian cell is an NSO cell.

179. (New) The method according to claim 117, wherein said mammalian cell is a CHO cell.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

180. (New) The method according to claim 117, wherein said mammalian cell is an NSO cell.

181. (New) The method according to claim 118, wherein said mammalian cell is a CHO cell.

182. (New) The method according to claim 118, wherein said mammalian cell is an NSO cell.

183. (New) The method according to claim 119, wherein said mammalian cell is a CHO cell.

184. (New) The method according to claim 119, wherein said mammalian cell is an NSO cell.

185. (New) The method according to claim 120, wherein said mammalian cell is a CHO cell.

186. (New) The method according to claim 120, wherein said mammalian cell is an NSO cell.

187. (New) The method according to claim 121, wherein said mammalian cell is a CHO cell.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

188. (New) The method according to claim 121, wherein said mammalian cell is an NSO cell.

189. (New) The method according to claim 122, wherein said mammalian cell is a CHO cell.

190. (New) The method according to claim 122, wherein said mammalian cell is an NSO cell.

191. (New) The method according to claim 125, wherein said mammalian cell is a CHO cell.

192. (New) The method according to claim 125, wherein said mammalian cell is an NSO cell.

193. (New) The method according to claim 126, wherein said mammalian cell is a CHO cell.

194. (New) The method according to claim 126, wherein said mammalian cell is an NSO cell.

195. (New) The method according to claim 128, wherein said mammalian cell is a CHO cell.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

196. (New) The method according to claim 128, wherein said mammalian cell is an NSO cell.

197. (New) The method according to claim 129, wherein said mammalian cell is a CHO cell.

198. (New) The method according to claim 129, wherein said mammalian cell is an NSO cell.

199. (New) The method according to claim 130, wherein said mammalian cell is a CHO cell.

200. (New) The method according to claim 130, wherein said mammalian cell is an NSO cell.

201. (New) The method according to claim 131, wherein said mammalian cell is a CHO cell.

202. (New) The method according to claim 131, wherein said mammalian cell is an NSO cell.

203. (New) The method according to claim 132, wherein said mammalian cell is a CHO cell.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

204. (New) The method according to claim 132, wherein said mammalian cell is an NSO cell.

205. (New) The method according to claim 133, wherein said mammalian cell is a CHO cell.

206. (New) The method according to claim 133, wherein said mammalian cell is an NSO cell.

207. (New) The method according to claim 136, wherein said mammalian cell is a CHO cell.

208. (New) The method according to claim 136, wherein said mammalian cell is an NSO cell.

209. (New) The method according to claim 137, wherein said mammalian cell is a CHO cell.

210. (New) The method according to claim 137, wherein said mammalian cell is an NSO cell.

211. (New) The method according to claim 149, wherein said mammalian cell is a CHO cell.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

212. (New) The method according to claim 149, wherein said mammalian cell is an NSO cell.

213. (New) The method according to claim 150, wherein said mammalian cell is a CHO cell.

214. (New) The method according to claim 150, wherein said mammalian cell is an NSO cell.

215. (New) The method according to claim 151, wherein said mammalian cell is a CHO cell.

216. (New) The method according to claim 151, wherein said mammalian cell is an NSO cell.

217. (New) The method according to claim 152, wherein said mammalian cell is a CHO cell.

218. (New) The method according to claim 152, wherein said mammalian cell is an NSO cell.

219. (New) The method according to claim 153, wherein said mammalian cell is a CHO cell.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

220. (New) The method according to claim 153, wherein said mammalian cell is an NSO cell.

221. (New) The method according to claim 154, wherein said mammalian cell is a CHO cell.

222. (New) The method according to claim 154, wherein said mammalian cell is an NSO cell.

223. (New) The method according to claim 155, wherein said mammalian cell is a CHO cell.

224. (New) The method according to claim 155, wherein said mammalian cell is an NSO cell.

225. (New) The method according to claim 173, wherein said mammalian cell is a CHO cell.

226. (New) The method according to claim 173, wherein said mammalian cell is an NSO cell.

227. (New) The method according to claim 174, wherein said mammalian cell is a CHO cell.

Application No. 10/612,497
Reply to March 15, 2005 Office Action
Reply Dated April 21, 2005

228. (New) The method according to claim 174, wherein said mammalian cell is
an NSO cell.

229. (New) The method according to claim 175, wherein said mammalian cell is
a CHO cell.

230. (New) The method according to claim 175, wherein said mammalian cell is
an NSO cell.